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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/711,896	11/15/2000	Tohru Kayano	KAYANO 1	8185

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EXAMINER
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ART UNIT	PAPER NUMBER
1645	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/711,896	Kayano et al.
Examiner	**Art Unit**
S. Devi, Ph.D.	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 16, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above, claim(s) *10-23* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-9 and 24-26* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *11.15.00* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☒ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *2 & 3.*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election

1) Acknowledgment is made of Applicants' election filed 04/16/03 (paper no. 11) in response to the restriction requirement mailed 03/17/03 (paper no. 10). Applicants have elected invention I, claim 5, along with linking claims 1-4, 6-9 and 24-26, with traverse. Applicants' traversal is on the grounds that the Office's restriction requirement appears to be an election of species requirement. Applicants state that MPEP § 803 requires that the PTO examine plural inventions if it would not constitute a serious burden to do so. Applicants contend that at least several of the designated species are sufficiently similar so that a search and examination of the additional species along with the search and examination of the closely similar elected species I would not constitute a serious burden. Applicants submit that the seven patentably distinct inventions set forth in the Office Action are so closely related as to be examined in a single application without undue burden on the Office.

Applicants' arguments have been carefully considered. As clearly set forth in the restriction requirement mailed 03/17/03 (paper no. 10), the various inventions claimed in the instant application were subject to a restriction requirement as opposed to a species election requirement. The two SEQ ID numbers recited in the claims are structurally distinct. A structural sequence search performed for one would not reveal all the relevant prior art on the other. The two patentably distinct antibodies have two distinct binding specificities. However, since Applicants have elected one of the two products, i.e., the product of invention I, the process claims corresponding to the scope of the product of invention I will be retained as pending claims pursuant to the rejoinder provisions of M.P.E.P 821.04 and will be withdrawn from consideration until such time as the subject matter of claim 5 is deemed allowable. The Examiner in charge of the instant application will then determine if the corresponding process claims include all of the limitations of the allowable product claim(s) and are of the same scope as allowable product claim(s), prior to determining if rejoinder will be permitted under M.P.E.P 821.04.

Status of Claims

2) Claims 1-26 are pending.

Claims 10-23 are withdrawn from consideration as being directed to non-elected inventions. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

The elected claim 5, drawn to an antibody specific to SEQ ID NO: 1, and the linking claims 1-4, 6-9 and 24-26 to the extent they encompass the elected subject matter, are under examination. A First Action on the Merits is issued for these claims.

Sequence Listing

3) Acknowledgment is made of Applicants' raw sequence listing and CRF filed 02/05/03 (paper no. 9) which have been entered.

Information Disclosure Statements

4) Acknowledgment is made of Applicants' information disclosure statements filed 03/09/01 (paper no. 3) and 03/21/01 (paper no. 2). The information referred to therein has been considered and a signed copy is attached to this Office Action (paper no. 12).

Priority

5) The instant specification claims foreign priority benefits under 35 U.S.C § 119 to the foreign application, 324860/1999 filed 11/16/199 in Japan.

Specification - Informalities

6) The specification is objected to for the following reason:

The use of the trademark in the instant specification has been noted. For example, see page 31, line 12: 'Sepharose'. The recitation should be capitalized wherever they appear and be accompanied by the generic terminology. Each letter of the trademark must be capitalized. See M.P.E.P 608.01(V) and Appendix l. Although the use of trademark is permissible in patent applications, the propriety nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Rejection(s) under 35 U.S.C § 101

7) 35 U.S.C. § 101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this cycle.

8) Claim 1 and those claims that depend from this claim are rejected under 35 U.S.C § 101 as being directed to a non-statutory subject matter.

Claim 1 is drawn to an antibody, and therefore reads on products of nature, i.e., naturally occurring antibody. The claim lacks limitations which distinguish this product from those that may

exist naturally. Consequently, the claim(s) does not embody patentable subject matter as defined in 35 U.S.C § 101. See MPEP 2105. The rejection can be obviated by amending claim 1 to recite --An isolated .... antibody-- in connection with the product to reflect the hands of the inventors in the production or creation of the recited product since such a recitation has descriptive support in the specification, as originally filed.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

9) Claims 1-9 and 24-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 24 lacks proper antecedent basis in the recitation "an antibody according to claim 1". Since claim 1 does not claim more than one antibody, it is suggested that Applicants provide proper antecedence by replacing the recitation with the recitation --the antibody of claim 1--.

(b) Claim 26 is vague, indefinite and confusing in the recitation: 'remedial, alleviative, or preventive agent for a disease relating to mature interleukin 18 or interleukin 18 precursor', because it is unclear what diseases are encompassed in the recitation: 'a disease relating to mature interleukin 18 or interleukin 18 precursor'. It is further not clear whether the remedial, alleviative or preventive ability of the antibody composition is towards the symptoms of the recited disease, the causative or infectious process itself of the disease, or the disease sequelae.

(c) Claims 1 and 3 are vague and indefinite in the recitation "a part ... of the amino acid sequence", because it is unclear what is encompassed in the recitation 'a part'. In the absence of size limitation on this 'part', the metes and bounds of the claim are indeterminate. How many amino acid residues in the recited amino acid sequence should be present in order to qualify as 'a part' of the amino acid sequence is not clear.

(d) Claim 2 is grammatically incorrect and/or confusing in the recitation "immunoreactivity .... is at most ten percent intensity of that against the precursor", because it is unclear what degree of immunoreativity in encompassed herein.

(e) Claim 5 is indefinite in that it encompasses non-elected subject matter.

(f) Claims 2-9 and 24-26, which depend directly or indirectly from claim 1, also stand rejected under 35 U.S.C. § 112, second paragraph, because of the vagueness or indefiniteness

identified above in the base claim.

Rejection(s) under 35 U.S.C § 102

10) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11) Claims 1-9 and 24-26 are rejected under 35 U.S.C. § 102(b) as being anticipated by Sana *et al.* (WO 97/44468).

Sana *et al.* disclosed monoclonal or polyclonal antibodies having binding affinity to, or being raised against a fragment of a human interleukin having the amino acid sequence of SEQ ID 2, or a homologous peptide. Diagnostic kits comprising the antibodies and buffers are taught (see page 24; paragraph bridging pages 23 and 24; and pages 5, 36, 37 and 47). One of the interleukin fragment is the prosequence of SEQ ID NO: 2 consisting of amino acids from position 1 (met) to position 36 (asp). See page 4. That this 36 amino acid-long prosequence of SEQ ID NO: 2 is structurally the same as the instantly recited SEQ ID NO: 1 is evident from SEQ ID NO: 2 depicted on page 54 of Sana *et al.*, which shows 100% sequence match between the instantly recited interleukin 18 precursor of SEQ ID NO: 1 and the fragment taught by Sana *et al.* Sana's antibodies are contained in physiologically acceptable carriers and are used in diagnostic assays or have therapeutic value (see pages 24, 32, 33 and 42). The antibodies are generated using the interleukin fragment as an immunogen for immunization of mammalian (i.e., warm-blooded) animals such as mice, rodents, primates, humans etc. (see paragraph bridging pages 23 and 24; and pages 32, 33 and 34). Hybridomas producing the monoclonal antibodies are taught (see page 34). The pharmaceutical composition comprising the antibody serves as an antagonist medicament in patients or individuals in need thereof (see claims and page 41). The antibodies are useful in the treatment of immunological disorders and conditions exhibiting abnormal interleukin expression (see page 40). Although Sana *et al.* do not recite the term 'interleukin 18 precursor', there is perfect structural sequence match to reasonably conclude that Sana's interleukin fragment is one and the same as the Applicants' interleukin 18 precursor. The functional limitation with regard to the percent intensity or immunoreactivity of the antibody is viewed as an inherent functional property inseparable from the

prior art antibody. Since the prior art interleukin fragment is structurally the same as the interleukin 18 precursor recited in the instant claims, an antibody to the same is expected to have the same immunological functions as that of the Applicants' antibody.

Additionally, it is noted that instant claims are product-by-process claims and are not limited to the manipulations of the recited steps, but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Any prior art antibody that has the recited structure and/or specificity irrespective of the process by which the antibody was produced would anticipate the instantly claimed antibody.

Claims 1-9 and 24-26 are anticipated by Sana *et al.*

12) Claims 1-6 and 24-26 are rejected under 35 U.S.C. § 102(b) as being anticipated by Akita *et al.* (*J. Biol. Chem.* 272: 26595-26603, October 1997).

Akita *et al.* disclosed monoclonal or polyclonal antibodies having binding affinity to prohIL-18 as tested by immunoblotting. The antibodies were raised in mice using recombinant hIL-18 (see Figure 6 footnote; and page 26601; 'Reagents and Antibodies' on page 26595). That an antibody used in immunoblotting would be contained in a buffer or saline (i.e., physiologically acceptable carrier) is inherent from the teachings of Akita *et al.* Akita *et al.* taught or identified the amino acid sequence of the prohIL-18 in Figure 2 as containing, MAAEPVEDNCINFVAMKFIDNTLYFAIEDDENLESD, which is identical in structure to the instantly recited SEQ ID NO: 1. The functional limitations with regard to the percent intensity or immunoreactivity of the antibody, or the IL-18 related disease-remedial, -alleviative or -preventive ability, is viewed as an inherent functional property inseparable from the prior art antibody. Since the prior art interleukin fragment is structurally the same as the interleukin 18 precursor recited in the instant claims, an antibody to the same is expected to have the same immunological or biological

functions as that of the Applicants' antibody.

Additionally, it is noted that instant claims are product-by-process claims and are not limited to the manipulations of the recited steps, but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Any prior art antibody that has the recited structure and/or specificity irrespective of the process by which the antibody was produced would anticipate the instantly claimed antibody.

Claims 1-6 and 24-26 are anticipated by Akita *et al.*

Rejection(s) under 35 U.S.C § 103

13) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person. having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

14) Claims 1 and 9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Akita *et al.* (*J. Biol. Chem.* 272: 26595-26603, October 1997).

The teachings of Akita *et al.* are described above, which do not teach an immunoassay kit comprising an antibody to interleukin 18 precursor.

However, methods of assembling an immunoassay kit using an art-disclosed product was well known and routinely practiced in the art, and would have been obvious to a skilled artisan at the time the invention was made to produce such a immunoassay kit for diagnostic purposes using the antibody of Akita *et al.* One of skill in the art would have been motivated to produce the instant invention for the expected benefit of making readily available Akita's antibody, or for commercializing Akita's antibody for diagnostic use, since it is routine and conventional to use antibody reagents in immunoassay kits.

Claims 1 and 9 are *prima facie* obvious over the prior art of record.

Remarks

15) Claims 1-9 and 24-26 stand rejected.

16) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1 (CM1). The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which receives papers 24 hours a day and seven days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

S. DEVI, PH.D.
PRIMARY EXAMINER

June, 2003